Irwin Freedberg: The Early Years at Harvard

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In 1959 Irwin Freedberg, after four years at Harvard Medical School and three years of residency at Beth Israel Hospital, arrived at Massachusetts General Hospital to begin his residency in dermatology. I, by chance, arrived at the same time, having attended the same medical school, interned at the old Peter Bent Brigham Hospital, and served as a medical officer in the field artillery during the Cold War. By the time our new chief, Thomas B. Fitzpatrick, arrived, we had already managed to shake up what had been a slightly complacent department because the previous chairman had been ill for a number of years. Irwin's and my first encounter with TBF was at skin rounds. This guy with a hand lens elbowed his way in and we elbowed him out in trying to examine a patient. At the end of rounds Tom was introduced as our new chief, and we both thought about looking for a new job. We spent two years learning the names of diseases and the limited therapies available. The clinic was a relatively easy rotation, because a number of part-time faculty also saw patients. The inpatient service was busier, because about 30 patients with extensive disease were managed by one first-year resident with limited experience and therapeutic options. As in all things that crossed Irwin's path, he did remarkably well. There were four residents, and we made consult rounds every Friday with Tom. At that time he repeatedly announced that we should work on the epidermis to balance his long-standing work on melanocytes, so really that is how it began. I still am not sure why, but Tom could not keep our names straight until after Irwin left.

Irwin thought we should begin a research career during our residency, and we decided to study the metabolic response to exfoliation; this was made possible by a metabolic ward, funded by the National Institutes of Health, at Massachusetts General Hospital. Fortunately the other residents were more experienced and could manage patients in greater numbers, so our occasional absences from the clinic were noticed but not a problem in terms of patient care. We had no difficulty finding patients with almost total-body psoriasis and made a suit, demonstrated in Figure 1 by Irwin, to collect scales. We spent part of every weekend aliquoting the stool collections, because that was not one of the core activities of the ward, and it was not a pleasant task. One good fallout of that project was that one of the nurses became interested in dermatology and worked on our White 8 Skin Service inpatient skin service for many years.

It was clear at the end of our first year that we needed training in basic science, and after reviewing all the programs in the Boston area, we decided to go to Brandeis, where Nate Kaplan had a program in biochemistry to train MDs in basic science without their having to go the PhD route. Fortunately there were training grants to fund our fellowship, since at that time we each had two kids to support. It was a turning point in our careers. Many others with a clinical background followed us, including residents from our own program. Although we continued to work on the epidermis together, our professional careers began to diverge. Irwin's exceptional personal skills became apparent, and his plans for the future were forming. After completing the fellowship, Irwin returned to Beth Israel. Over the years we continued to interact with our earlier mentors, and we were members of the Brandeis Club.

Figure 1. Irwin Freedberg demonstrates a suit for collecting psoriasis scales at Massachusetts General Hospital.

Irwin started a clinical and research program, the first in dermatology separate from Massachusetts General Hospital, at Beth Israel. He attracted additional outstanding faculty, both in the clinical area and in research, who built strong programs of their own under his mentorship. In 1969 he was awarded a John Guggenheim Memorial Foundation Fellowship at the Department of Biophysics of Weizmann Institute of Science, with the renowned protein chemist Ephraim Katchalski-Katzir, to enhance his research skills. He became head of the department at Beth Israel and a tenured professor at Harvard Medical School.

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He recognized the need for more leadership at the teaching hospitals proximal to Beth Israel and Harvard Medical School and developed the program at the Boston Children's Hospital, where he was made chief of the Division of Dermatology at the Children's Hospital Medical Center and dermatologist at the Boston Hospital for Women.

When Irwin announced he was leaving Harvard, I was in disbelief. Why would he give up such a successful position, by then in a rapidly growing prestigious program? We both had looked at other job offers, but in my case mostly as an ego trip. These past two years before and since his death I have thought a lot more about what the Boston experience was about and how it molded him. The years at Harvard were like basic training, and Irwin had strong role models in academia in and outside of dermatology at Beth Israel and Harvard Medical School. He was ambitious, but in a very special way. He was confident about himself and his ideas of where dermatology and skin research should move. He felt he could put ideas into action by attaining leadership positions in the organizations that established or influenced policy in the clinical and research areas, such as the Society for Investigative Dermatology, the American Academy of Dermatology, the American Dermatological Association, and the National Institutes of Health. Irwin eventually assumed leadership positions in the Society for Investigative Dermatology and was editor of the *Journal of Investigative Dermatology*. He had the people skills, which are critical for such an undertaking, but I think he felt he needed the platform of chairmanship at a strong university to carry out his ideas. With Tom Fitzpatrick firmly in place at Harvard, moving to another institution was a necessity. Irwin already had leadership experience and was known and respected in the scientific community, and taking over a program would not be unduly challenging to someone with his ability, energy, and healthy self-esteem. Furthermore, his personal life with his children and his wife Irene was rock solid. When I look at pictures of Irwin from our medical school years at Harvard and New York University, I see the same man but with different ambitions and academic research accomplishments. The outpouring of emotion at his passing was not merely for the friend whom we loved and who left us too soon but was also an expression of gratitude for the man who contributed so much to the growth of dermatology as a clinical specialty and science.

Irwin Freedberg: Keratins Before the Beginning

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It was through my meeting Bill Montagna in Cambridge, UK, in 1955 that I met Irwin Freedberg some eight years later. It happened this way.

In 1954, when Irwin would have been in the middle of his medical studies at Harvard, I was a research student in Cambridge, UK. I was using the new electron microscope techniques of Porter and Palade to investigate hair ultrastructure and to see if biochemical information could be correlated with it. Montagna was working in London with Geoffrey Bourne; I had published some work using the new tetrazolium salts, and for that reason he visited me in Cambridge. That meeting and subsequent friendship initiated my entrée into the bigger world of investigative dermatology in the USA to view the excitement about basic research on skin hallmarked by Stephen Rothman's 1954 book, *Physiology and Biochemistry of the Skin*.

Montagna invited me to his 1959 meeting in New York on Hair Growth and Hair Regeneration when Irwin would have begun his dermatology residency at Massachusetts General Hospital. However, it was not until 1963 at the Lake Arrowhead conference organized by Montagna and Lobitz (published as Montagna and Lobitz, 1964) that I met him. Irwin Freedberg was one of a group of young investigative dermatologists, including Howard Baden, who were present at the conference and entering the new era of keratinology. The conference was a landmark because the invitees included older and newer faces in the field, the older including Stephen Rothman, Honor Fell, Howard Mercer, Elizabeth Hay, Albert Kligman, Izzy Bernstein, Eugene van Scott, Peter Flesch, and Ruth Freinkel, covering a wide range of the biology of skin — I was somewhere in between.

Howard Mercer and Birbeck in 1957 published their work on the ultrastructure of the hair follicle and had visualized cortical filaments, or microfibrils as they were then called. Their findings, incidentally, confirmed Mercer's conclusion, made in the 1940s from his viewing degraded wool fibers on a grid in one of the first postwar electron microscopes, that the fiber cortex was an admixture of filaments with a matrix. In 1959, I made the matrix more reactive with osmium and lead in ultrathin sections of mature wool and hair fibers and other "hard" keratins such as nail, horn, and echidna quills, thereby enhancing contrast and visualization of the ultrastructure of mature hard keratins. Because of the narrowed focus on them, several years had to pass before it was realized that the microfibrils of wool, hair, and hard keratins generally, were members of the wider family of intermediate filaments.

Hard keratins were solubilized by Goddard and Michaelis in 1937, but

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